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s polymor(w)mucin or hpem

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S3	1044	S2 AND POLYMORPH?
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1: J Biol Chem 1988 Sep 15;263(26):12820-3

Related Articles, Nucleotide, Protein, Books, LinkOut

A highly immunogenic region of a human polymorphic epithelial mucin expressed by carcinomas is made up of tandem repeats.

Gendler S, Taylor-Papadimitriou J, Duhig T, Rothbard J, Burchell J.

Imperial Cancer Research Fund, London, United Kingdom.

The nucleotide sequences of partial cDNA clones coding for the core protein of a human polymorphic epithelial mucin were determined, and a large domain was found to consist of a 60-base pair tandem repeat sequence. The cDNA clones were originally selected (Gendler, S. J., Burchell, J. M., Duhig, T., Lamport, D., White, R., Parker, M., and Taylor-Papadimitriou, J. (1987) Proc. Natl. Acad. Sci. U. S. A. 84, 6060-6064) using three monoclonal antibodies which show differential reactivity with the mucin produced by normal and malignant breast. Two of the epitopes are exposed in the normally processed and cancer-associated mucin, while one epitope is unmasked only in the cancer-associated mucin (Burchell, J. M., Durbin, H., and Taylor-Papadimitriou, J. (1983) J. Immunol. 131, 508-513; Burchell, J., Gendler, S., Taylor-Papadimitriou, J., Girling, A., Lewis, A., Millis, R., and Lamport, D. (1987) Cancer Res. 47, 5476-5482). We show here that all three antibodies react with a synthetic peptide with an amino acid sequence corresponding to that predicted by the tandem repeat. Identification of the epitopes preferentially expressed on the cancer-associated mucin should allow a directed approach to the development of tumor-specific antibodies using synthetic peptides as immunogens.

PMID: 3417635 [PubMed - indexed for MEDLINE]
1: Proc Natl Acad Sci U S A 1987 Sep;84(17):6060-4

Cloning of partial cDNA encoding differentiation and tumor-associated mucin glycoproteins expressed by human mammary epithelium.

Gendler SJ, Burchell JM, Duhig T, Lamport D, White R, Parker M, Taylor-Papadimitriou J.

Human mammary epithelial cells secrete and express on their cell surfaces complex mucin glycoproteins (Mr greater than 250,000) that are developmentally regulated, tumor-associated, and highly immunogenic. Studies using monoclonal

antibodies directed to these glycoproteins suggest that their molecular structures can vary with differentiation stages in the normal gland and in malignancy. To analyze the molecular nature of these glycoproteins, milk mucin was affinity-purified and deglycosylated with hydrogen fluoride, yielding bands at 68 and 72 kDa on silver-stained gels.

Polyclonal and monoclonal antibodies to the stripped core protein were developed and used to screen a lambda gt11 expression library of cDNA made from mRNA of the mammary tumor cell line MCF-7. Seven cross-reacting clones were isolated, with inserts 0.1-1.8 kilobases long. RNA blot analysis, using as a probe the 1.8-kilobase insert subcloned in plasmid pUC8 (pMUC10), revealed transcripts of 4.7 and 6.4 kilobases in MCF-7 and T47D mammary tumor cells, whereas normal mammary epithelial cells from pooled milks have additional transcripts. The expression of mRNA correlates with antigen expression as determined by binding of two previously characterized anti-mucin monoclonal antibodies (HMFG-1 and HMFG-2) to seven cell lines. Restriction enzyme analysis detected a restriction fragment length polymorphism when human genomic DNA was digested with EcoRI or HinfI.